their vicinity is turbulent, they are ideal sites for harboring infective organisms. Consequently, infective endocarditis, on either the aortic valve or the membrane itself, is common in this condition.[2,3] In the series analyzed by Wright et al,[2] infective endocarditis occurred in 10 (12%) of 83 patients with discrete subaortic stenosis, with a frequency of 14.3 cases per 1,000 patient-years. Frequencies of infective endocarditis occurring in aortic valvular stenosis and ventricular septal defect were 0.8 and 1.5 cases per 1,000 patient-years, respectively.[10] Thus, it is likely that discrete subaortic stenosis is the cardiac condition most frequently complicated by infective endocarditis.[3]

Occasionally, the infection spreads from the aortic valve and involves the aorta, resulting in the formation of mycotic aneurysm.[3] To our knowledge, isolated infective aortitis in discrete subaortic stenosis with perforation and resulting hemopericardium, as in the present case, has never been described in the English language literature. In this case, the jet of blood probably impinged on both the aortic leaflets and the aortic root immediately above these leaflets, as evidenced by fibrous thickening and close anatomic relation of these structures (Figures 1 and 2). Accordingly, the damaged aortic intima, along with the thickened aortic leaflets, was at an increased risk for infective arteritis. The infective organism in this case was *Staphylococcus aureus*, a highly virulent bacterium, accounting for the rapid downhill clinical course.

Finally, it is worth emphasizing that discrete membranous subaortic stenosis is a progressive lesion. The fibroelastic process extends both proximally along the ventricular septum and distally toward the base of the aortic leaflets,[11] contributing in part to the development of aortic regurgitation and progressive severity of the obstruction.[2,5] Due to the high risk of invective endocarditis and aortitis and the relentless progression in the degree of obstruction, we agree with Somerville et al in that surgical resection of the obstructive band should be contemplated at the earliest possible moment.[12]

REFERENCES

1. Katz NM, Buckley MJ, Liberthson RR. Discrete membranous subaortic stenosis—report of 31 patients, review of literature, and delineation of management. Circulation 1977; 56:1034–1038

2. Wright GB, Keane JF, Nadas AS, Bernhard WF, Castaneda AR. Fixed subaortic stenosis in the young: medical and surgical course in 83 patients. Am J Cardiol 1983; 52:830–835

3. Roberts WC. Adult Congenital Heart Disease. Philadelphia, Penn, FA Davis, 1987, pp 656–659

4. Mugge A, Daniel WG, Wolpers HG, Klopper JW, Lichtlen PR. Improved visualization of discrete subvalvular aortic stenosis by transesophageal color-coded Doppler echocardiography. Am Heart J 1989; 117:474–475

5. Freedom RM, Pelech A, Brand A, et al. The progressive nature of subaortic stenosis in congenital heart disease. Int J Cardiol 1985; 8:137–143

6. Douville EC, Sade RM, Crawford FA Jr, Wiles HB. Subvalvular aortic stenosis: timing of operation. Ann Thorac Surg 1990; 50:29–33

7. DeVries AG, Hess J, Witsenburg M, Frohn-Mulder IM, Bogers JJ, Bos E. Management of fixed subaortic stenosis: a retrospective study of 57 cases. J Am Coll Cardiol 1992; 19:1013–1017

8. Brown J, Stevens L, Lynch L, et al. Surgery for discrete subvalvular aortic stenosis: actuarial survival, hemodynamic results, and acquired aortic regurgitation. Ann Thorac Surg 1985; 40:151–155

9. Lababidi Z, Weinhaus L, Stoeckle H Jr, Walls JT. Transluminal balloon dilatation for discrete subaortic stenosis. Am J Cardiol 1987; 59:423–425

10. Gersony WM, Hayes CJ. Bacterial endocarditis in patients with pulmonary stenosis, aortic stenosis, or ventricular septal defect. Circulation 1977; 56(suppl I):I84–I87

11. Feigl A, Feigl D, Lucas RV Jr, Edwards JE. Involvement of the aortic valve cusps in discrete subaortic stenosis. Pediatr Cardiol 1984; 5:185–190

12. Somerville J, Stone, S. Ross DR. Fate of patients with fixed subaortic stenosis after surgical removal. Br Heart J 1980; 43:629–647

Adrenomyeloneuropathy Presenting in Adulthood

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ADRENOLEUKODYSTROPHY (ALD) is an inherited metabolic disorder characterized by adrenal insufficiency, demyelination of the nervous system, and elevated levels of saturated very long chain fatty acids (VLCFAs).[1–3] The more common form of ALD is X-linked and occurs in childhood or adolescence; however, a neonatal form occurs from autosomal recessive inheritance. Most patients are diagnosed in childhood or adolescence when they have such neurologic manifestations as cognitive dysfunction, behavioral problems, changes in vision, or seizures.[2,3] The accompanying neurologic disease progresses rapidly, and dementia, blindness, and inability to speak or move with purpose may develop within a few years.[3]

Adrenomyeloneuropathy (AMN) is a distinct clinical form of ALD. Patients with AMN tend to be older, with onset of the disease typically occurring in adolescence or adulthood.[4] It is a progressively slower form of ALD, and patients may survive well into adulthood.[4] The spinal cord and peripheral nerves are initially affected more severely than the cerebral white matter; thus, findings commonly include lower extremity spasticity, weakness, and sensory disturbances.[2,3] Urinary retention and impotence often develop.[2,3] Later manifestations include cerebellar ataxia (with staggering and difficulty of willed movements) and intellectual deterioration.[4]

The underlying metabolic defect in the X-linked forms of ALD is the inability to normally oxidize VLCFAs because of the impairment of the peroxisomal enzyme, lignoceryl-coenzyme A ligase.[2,3] As a result, saturated fatty acids with a carbon chain length of at least 24 accumulate in various tissues—including the adrenal gland, brain, and spinal cord. The diagnosis of ALD is made by measuring VLCFAs C24:0 and C26:0 and their ratios to C22:0.[1–3]

The case reported here involves a 24-year-old man—diagnosed at age 10 with idiopathic primary adrenal insufficiency—who presented with weakness and spas-

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ticity of the lower extremities. His clinical presentation supported the diagnosis of AMN, and this was confirmed by measurement of VLCFAs. His case illustrates two points: that many years can pass between the onset of the adrenal component and the onset of the neurologic component of ALD; and that when primary adrenal insufficiency is diagnosed in a male who appears to be neurologically normal, it is possible that the adrenal insufficiency is due to ALD. It is thus important to consider this metabolic disorder in any young man with apparent idiopathic primary adrenal insufficiency.

Report of a Case

The patient was well until the age of 10, when he presented with fatigue, weakness, nausea, and darkening of his skin. At that time, he was diagnosed with primary adrenal insufficiency. Treatment with daily hydrocortisone and fludrocortisone acetate was started, and he remained otherwise well. At age 24, he presented to the clinic with leg weakness and difficulty walking up stairs. Six months later, his problem had progressed, and he presented with leg numbness, occasional difficulty with incontinence. He said that he had been "walking funny." The patient was admitted to the medicine service for evaluation and given hydrocortisone and Flourinef.

His vital signs were as follows: blood pressure 112/82 mm of mercury, pulse 82 beats per minute, and temperature 37.1° C (98.8° F). His skin was dark, especially in the palmar creases and on the buccal mucosa. The results of a cranial nerve examination were normal. Muscle strength levels were normal in the upper and lower extremities except for weakness of the peroneal muscles. In his lower extremities, the tone was spastic and deep tendon reflexes were enhanced; a positive Babinski reflex was also present. There was decreased pinprick sensation in his feet. His gait was broad based, and spastic ataxia with scissoring was noted.

The patient's laboratory evaluation included normal a serum level of electrolytes and nonreactive RPR. His HIV serologic tests were negative. A lumbar puncture was normal. The results of a head CT scan and thoracic and lumbar-sacral myelograms were normal.

The neurology service was consulted. They suggested that the patient had AMN, a phenotypic variant of ALD. Plasma VLCFAs were measured. The C26:0 level was 1.030 µg per ml (normal, 0.118 to 0.526); the C26:0 to C22:0 ratio was 0.092 (normal, 0.007 to 0.023); and the C24:0 to C22:0 ratio was 1.446 (normal, 0.706 to 1.006). These values confirmed the presence of ALD.

The patient's last clinic visit was five months later. His leg weakness had progressed to the point that he was wheelchair-bound.

Discussion

Although there are many etiologies of primary adrenal insufficiency, practically all are attributable to either autoimmune adrenal failure (about 75% to 80%) or tuberculosis (about 20%).[1] Other etiologies such as ALD are thought to be distinctly uncommon and to amount to only a fraction of the cases.[1]

A recent study found that out of eight males with childhood-onset Addison's disease and no signs or symptoms of neurologic dysfunction, five had the biochemical defect of ALD and clear evidence (by MRI examination) of ALD involving the brain.[5] In another study of a group of 59 French children with Addison's disease , 23 (39%) were diagnosed with ALD.[6] Although these studies involve small numbers of patients, their findings suggest that ALD may account for a larger proportion of patients with recognized adrenal insufficiency.

As the patient's case reported here demonstrates, ALD often is not suspected until both primary adrenal insufficiency and neurologic abnormalities are detected.[3] The two problems, however, may appear at different times in the course of ALD. The time between the onset of adrenal insufficiency and the onset of overt neurologic manifestations may be years; in fact, 14 years passed between onsets in the patient in this report.[3,4,7] Although adrenal insufficiency may exist, physicians may not consider the diagnosis of ALD when neurologic symptoms are nonexistent and neurologic function appears to be normal. Therefore, a factor that could lead to underestimation of the incidence of ALD is that patients who initially appear to have "idiopathic" adrenal insufficiency may in time be found to have ALD as the cause of adrenal failure. In addition, even when neurologic manifestations are evident, ALD may be underdiagnosed simply because of a lack of awareness of this unusual disorder. If this is the case, a patient with ALD could be thought to have two distinct underlying disorders—primary adrenal insufficiency and a primary neurologic disease. Our patient's presentation to clinic as a 24-year-old with leg weakness and difficulty climbing stairs should have prompted consideration of the diagnosis of AMN. This possibility was initially overlooked, and his diagnosis was delayed until six months later, when his symptoms had progressively worsened.

Identifying ALD as the cause of adrenal insufficiency is important because the neurologic component of the disease is progressive and eventually fatal.[3] Thus, the prognosis of primary adrenal insufficiency associated with ALD is far worse than most other etiologies. ALD is an inherited metabolic disease; other family members are at risk for developing it or being a carrier and should be identified. There is no proven standard treatment for the neurologic component of ALD. Some studies regarding diet and bone marrow transplantation, however, have given encouragement that ALD may be responsive to treatment, especially if started early in the course of the disease.[2,8,9] Because VLCFA accumulation is evident at an early age, patients with ALD can be diagnosed even when neurologic symptoms are minimal or absent.[3]

Our patient illustrates that when primary adrenal insufficiency is diagnosed in a man with apparently normal neurologic status, it is possible that the adrenal insufficiency is a manifestation of ALD. Recent studies

suggest that ALD may occur more commonly than we have acknowledged, which emphasizes the importance of considering this disorder in any young man with apparent idiopathic primary adrenal insufficiency. It may be valuable to screen all such patients for ALD.

REFERENCES

1. Miller WL, Tyrrell JB. The adrenal cortex. In Felig P, Baxter JD, Frohman LA (Eds): Endocrinology and Metabolism (3rd edition). New York, NY, McGraw-Hill, 1995, 555–771

2. Moser HW, Bergin A, Naidu S, Ladenson PW. Adrenoleukodystrophy. Endocrinol Metab Clin North Am 1991; 20:296–318

3. Rizzo WB. X-linked adrenoleukodystrophy: a cause of primary adrenal insufficiency in males. The Endocrinologist 1992; 2:177–183

4. Griffin JW, Goren E, Schaumburg H, Engel WK, Loriaux L. Adrenomyeloneuropathy: a probable variant of adrenoleukodystrophy. Neurology 1977; 27:1107–1113

5. Sadeghi-Nejad A, Senior B. Adrenomyeloneuropathy presenting as Addison's disease in childhood. N Engl J Med 1990; 322:13–16

6. Aubourg P, Chaussain JL. Adrenoleukodystrophy presenting as Addison's disease in children and adults. Trends Endocrinol Metab 1991; 2:49–52

7. Ladenson PW. Adrenoleukodystrophy. JAMA 1989; 262:1504–1506

8. Moser AB, Borel J, Odone A, et al. A new dietary therapy for adrenoleukodystrophy: biochemical and preliminary clinical results in 36 patients. Ann Neurol 1987; 21:240–249

9. Aubourg P, Blance S, Jahnbaqúe I, Kalifa G, et al. Reversal of early neurologic and neuroradiologic manifestations of X-linked adrenoleukodystrophy by bone marrow transplant. N Engl J Med 1990; 322:1860–1866.

Pulmonary Microvascular Cytology for the Diagnosis of Pulmonary Tumor Embolism

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PULMONARY TUMOR EMBOLISM (PTE) occurs when aggregates of tumor cells lodge in the pulmonary microvasculature. PTE can cause various clinical manifestations, including hypoxemia, dyspnea, pulmonary hypertension, acute cor pulmonale, and death in patients with cancer. We report on two patients who had precipitous terminal courses of respiratory failure—the first caused by extensive pulmonary tumor emboli resulting in fulminant cor pulmonale and the second by lymphangitic carcinomatosis. Pulmonary microvascular cytology sampling was an important diagnostic tool in both patients.

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Report of Cases

Patient 1

A 39-year-old woman with a history of breast cancer was admitted with rapidly progressive shortness of breath and hypotension. She was empirically begun on intravenous heparin because of the clinical suspicion of pulmonary emboli.

On physical examination, the patient's vital signs were as follows: pulse 122 beats per minute; blood pressure 89/57 mm of mercury; respiratory rate 44 breaths per minute; and temperature 38.4°C (101.1°F). Physical examination revealed the patient to be in moderate respiratory distress and intermittently confused. Cardiopulmonary examination revealed jugular venous distention, tachycardia, and clear lung fields. Abdominal examination revealed mild right upper quadrant tenderness and hepatomegaly. The extremity exam revealed 2+ pitting edema without clubbing.

A chest radiograph revealed a moderately enlarged heart with right lower lobe patchy consolidation (Figure 1). Her laboratory test results indicated metabolic acidosis, severe hypoxemia, and microangiopathic hemolytic anemia.

An echocardiogram revealed a moderately dilated right ventricle with severe right ventricle failure and no evidence of tamponade. A pulmonary artery catheter was inserted to aid in hemodynamic monitoring and vasopressor therapy. The hemodynamic data revealed a cardiac output of 3.4 liters per minute, central venous pressure of 20 mm of mercury, pulmonary capillary wedge pressure of 10 mm of mercury, and a pulmonary artery pressure of 59/31 mm of mercury. A ventilation-perfusion scan revealed a matched nonsegmental defect in the left lower lobe, which was interpreted as low probability for pulmonary embolism.

With the patient's history of breast cancer, acute right ventricular failure, and microangiopathic hemolytic anemia, pulmonary tumor emboli was believed to be a strong diagnostic consideration. A pulmonary microvascular cytology specimen was obtained from the distal port of the pulmonary artery catheter and revealed carcinoma, confirming the diagnosis of tumor emboli (Figure 2, left).

Despite aggressive hemodynamic support and attempted treatment of the tumor, the patient died of refractory cardiogenic shock within 24 hours of admission. At autopsy, the heart weighed 250 grams and had moderate dilatation of the right ventricle without hypertrophy. The tricuspid valve was dilated at 12 cm. The lungs grossly showed small deposits of metastatic carcinoma in her pleural and parenchymal lymphatics and a recent hemorrhage in the lingula. No pulmonary thromboemboli were present. Through microscopic examination, the majority of small pulmonary arteries showed plugging by nests of carcinoma (Figure 2, right) or neoplastic cells associated with proliferating young fibrous tissue—corresponding to carcinomatous arteriopathy. Extensive metastatic carcinoma was present in the liver; small